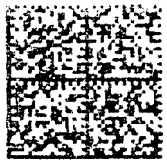
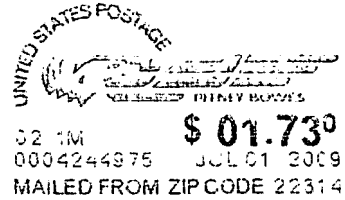
IC16UU REMSEN

Organization_____ Bldg/Room_____

United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
If Undeliverable Return in Ten Days

OFFICIAL BUSINESS
PENALTY FOR PRIVATE USE, $300





AN EQUAL OPPORTUNITY EMPLOYER

Cool 200

COOL200* 20036[illegible] 1408 13 07/09/09
FORWARD TIME [illegible] N TO SEND
:COOLEY GODWARD [illegible]
777 6TH ST NW [illegible] 850
WASHINGTON DC 20001-3714

RETURN TO SENDER

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,377	06/19/2006	Catherine J. Pachuk	NUCL-006/01US 306512-2111	3823

7590 07/01/2009

COOLEY GODWARD KRONISH LLP
ATTN: Patent Group
5th Floor
1200 19th Street, NW
Washington, DC 20036

EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
07/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,377	PACHUK ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/12/09 & 3/17/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-79 and 82-97* is/are pending in the application.

4a) Of the above claim(s) *32-62,68-77 and 82-97* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-67,78 and 79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/27/06;2/27/07;3/21/07;2/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *seq alignment*.

DETAILED ACTION

Restriction election

1. Applicant's election, with traverse, of Group IV and SEQ ID NOs: 3 and 10, in the reply on December 12, 2008, in acknowledged.

2. The traverse is on the ground(s) that SEQ ID NOs: 18-22 and 54-58 of Group I share substantial sequence identity to the two elected sequences. Applicants request that these sequences also be examined.

3. This argument is not persuasive. First, this application is national stage of PCT/US04/19229, filed on June 10, 2004, in which only SEQ ID NOs 1-48 was filed. The claimed SEQ ID NOs: 54-58 do not appear to be originally filed, also see Para 5 below. Secondly, SEQ ID NOs: 18-22 and 54-58 appear to have different sequences from the elected SEQ ID NOs: 3 and 10. Applicant has failed to provide a sequence comparison showing that they are substantially the same as claimed. Finally, simultaneous search and examination of multiple sequences constitutes a serous burden to the Office. Alternatively, structurally-related molecules are searched and examined using the approach of examining Applicant's preferred species first, and then genus (see MPEP 803.02). Thus, when the elected sequences are found allowable, the substantially same sequences as the elected sequence could be rejoined for examination if Applicant provides a sequence comparison showing that the additional sequences as originally filed are substantially the same as claimed. The requirement of restriction is still deemed proper, and is therefore made FINAL.

4. Accordingly, Claims 32-79 and 82-97 are pending. Claims 53-62, 68-77 and 82-97 have been withdrawn by Applicant. Claims 32-52 are withdrawn from further consideration by the

Examiner, under 37 C. F. R. 1.142(b), as being directed to a nonelected invention. Claims 63-67 and 78-79 are examined in this Office action.

Specification

New Matter

5. The amendments filed on December 12, 2005, and June 19, 2006, are objected to under 35 U.S.C. 132(a) because they introduce new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. This application is national stage of PCT/US04/19229, which contains SEQ ID NO:1-48. It is noted that Applicant submitted a new Fig. 15, and a new sequence list along with the new version of the specification on December 12, 2005, which contain an additional 28 new sequences that were not present in both PCT/US04/19229 and 60/478,076. Applicant also submitted a new version of the specification on December 12, 2005, which appears to be different from the original specification of PCT/US04/19229. A marked-up copy of the new version of the specification was not submitted alone with a clear-copy.

6. It is further noted that more new sequences were introduced by the amendment dated June 19, 2006. Applicant also failed to submit a marked-up copy of the amendment to the specification on

7. Applicant is required to **cancel any new matter,** or point to specific support in the original specification for the additions and changes in the amendment, in the reply to this Office action. Applicant is also required to submit both marked-up copy and clear copy of the amendment for review and record.

8. The use of trademarks has been noted in this application, e.g. Lipofectamine™, Opti-MEM™, Auszyme™ and Rneasy™ throughout the text. Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Correction is required.

Priority

9. This application is national stage of PCT/US04/19229, filed on June 10, 2004, and claims priority over 60/478,076, filed on June 12, 2003. A review of the priority document shows support for SEQ ID NO: 3, but not SEQ ID NO: 10. Therefore, the priority date for a method of use of SEQ ID NO: 3 has been currently determined to be June 12, 2003. The priority date for a method of use of SEQ ID NO: 10, or use of both SEQ ID NOs: 3 and 10 has been currently determined to be June 10, 2004.

Information Disclosure Statement

10. The information disclosure statements submitted on December 27, 2006, February 27, 2007, March 21; 2007, and February 19, 2008, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the

basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 63 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Ill (US 5,843,770).

13. Claims 63 and 78 are directed to a composition and a method for inhibiting expression of a polynucleotide sequence of hepatitis B virus in an *in vivo* mammalian cell comprising administering to said cell a double-stranded RNA (dsRNA) effector molecule **comprising** an at least 19 contiguous base pair nucleotide sequence from within a sequence selected from the group consisting of SEQ ID NO: 3 and SEO ID NO: 10, wherein U is substituted for T. The specification Para [0049] provides following definition of dsRNA effector molecule:

[0049] "By "dsRNA" is meant a nucleic acid containing a region of two or more nucleotides that are in a double stranded conformation. It is envisioned that the conserved viral sequences of the invention may be utilized in any of the many compositions known in the art or subsequently developed which act through a dsRNA-mediated gene silencing or RNAi mechanism. In various embodiments, **the dsRNA consists entirely of ribonucleotides or consists of a mixture of ribonucleotides and deoxynucleotides. ..., The dsRNA may be a single molecule with a region of self-complementarity such that nucleotides in one segment of the molecule base pair with nucleotides in another segment of the molecule**. In various embodiments, a dsRNA that consists of a single molecule consists entirely of ribonucleotides or includes a region of ribonucleotides that is complementary to a region of deoxyribonucleotides. Alternatively, the **dsRNA may include two different strands that have a region of complementarity to each other**. In various embodiments, both strands consist entirely of ribonucleotides, one strand consists entirely of ribonucleotides and one strand consists entirely of deoxyribonucleotides, or one or both strands contain a mixture of ribonucleotides and deoxyribonucleotides....In some embodiments, the dsRNA does not contain any single stranded regions, such as single stranded ends, or the dsRNA is a hairpin. In other embodiments, the dsRNA has one or more single stranded regions or overhangs. Desirable RNA/DNA hybrids include a DNA strand or region that is an antisense strand or region (e.g, has at least 70, 80, 90, 95, 98, or 100% complementarity to a target nucleic acid) and an RNA strand or region that is a sense strand or region (e.g, has at least 70, 80, 90, 95, 98, or 100% identity to a target nucleic acid). In various embodiments, the RNA/DNA hybrid is made in vitro using enzymatic or chemical synthetic methods such as those described herein or those described in WO 00/63364, filed Apr. 19, 2000. In other embodiments, a **DNA strand synthesized in vitro is complexed with an RNA strand made in vivo or in vitro before, after, or concurrent with the transformation of the DNA strand into the cell**. In yet other embodiments, **the dsRNA is a single circular nucleic acid containing a sense and an antisense region**, or the dsRNA includes a circular nucleic acid and either a second circular nucleic acid or **a linear nucleic acid**.

[0073]The term "in vivo" is intended to include any system wherein the cellular DNA or RNA replication machinery

is intact, including **tissue culture systems**, and within single cell or multicellular living organisms.

14. In view of the specification, the claimed dsRNA can be in a form of double stranded DNA, DNA/RNA hybrid, single stranded DNA or RNA. The term "in vivo" includes **tissue culture systems**, and within single cell or multicellular living organisms.

15. Ill teaches a method of inhibiting HBV in mice using antisense SEQ ID NO: 1 of HBV viral cis-acting post-transcriptional regulatory sequences ("PREs"), see e.g. Abstract, line 15-25, col. 2, and line 10-58, col. 11. The antisense SEQ ID NO: 1 of the prior art comprises "at least 19 contiguous base pair nucleotide sequence of the claimed dsRNA SEQ ID NO: 10, see attached sequence alignment, wherein U is substituted for T." In view of the definition of dsRNA recited above, Ill's antisense to PRE and the method of inhibiting HBV *in vivo* meet the limitation of the claims, therefore anticipates Claims 67 and 78.

16. Claims 63 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Sallberg (US20020155124, published on October 24, 2002: Now US Pat. 6,680,059).

17. Sallberg teach methods of enhancing the immune response of an animal, including humans, using HBV nucleic acid-based antigen and antiviral drug Ribavirin, wherein said nucleic acid-based antigens include a nucleotide sequence of HBV SEQ ID No: 14, see e.g. [0017] and [0041]. Sallberg also teaches that a nucleic acid-based antigen can comprise at least 9-25, 25-50, 50-100, 100-200, 200-500, 500-1000, 1000-2000, or 2000-4000 consecutive nucleotides of any one of SEQ ID NO: 14 or an RNA that corresponds to these sequences. The nucleic acid-based antigen SEQ ID NO: 14 of the prior art comprises "a double-stranded RNA

effector molecule **comprising** an at least 19 contiguous base pair nucleotide sequence... SEQ ID NO: 3, wherein U is substituted for T" (Claims 63 and 78), See attached sequence alignment. Sallberg teaches that HBV nucleic acid-based antigen, including SEQ ID NO:14 and its fragments, is cloned into an expression vector, see e.g. Para [0040].

18. Sallberg has inherently taught the claimed dsRNA. As defined by the specification Para [0049], the claimed dsRNA effector molecule can be in form of a double stranded DNA, DNA/RNA hybrids, or a single stranded RNA. Given that the HBV nucleic acid-based antigen comprising SEQ ID NO: 14 and its fragments of the prior art is in form of double stranded DNA, and they can form DNA/RNA hybrids, or mRNA (a single stranded RNA) *in vivo*, the HBV nucleic acid-based antigens of the prior art meet the structural limitation of the claimed dsRNA effector molecules. Thus, Sallberg's method of using the HBV nucleic acid-based antigen comprising SEQ ID NO: 14 and its fragments for inhibiting HBV *in vivo* anticipate the claimed instant Claims 63 and 78.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering the patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of their obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 63-67, 78 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ill (US 5,843,770), Sallberg (US2002/0155124), and McCaffrey (Nature Biotechnology, 21(6):639-644; published online May 12, 2003, cited in IDS).

21. Claims 63 and 78 have been summarized *supra*. Claims 64-67 require a composition comprising two dsRNAs SEQ ID NOs: 3 and 10, and a method of inhibiting HBV *in vivo* using dsRNAs SEQ ID NOs: 3 and 10.

22. The relevance of Ill is set forth *supra*. In addition, Ill teaches that the antisense construct is an expression plasmid encoding **one** or **more** antisense transcripts (dsRNA effector molecule) which hybridize under intracellular conditions to all or a portion of a viral PRE within a viral transcript. The antisense constructs can be used to inhibit viral production, such as HBV production.

23. However, Ill does not teach use of two dsRNA comprises an at least 19 contiguous base pair nucleotide sequence from within SEQ ID NOs: 3 and 10.

24. The relevance of Sallberg is set forth *supra*.

25. McCaffrey teaches RNAi (dsRNA) can be applied to inhibit production of HBV replicative intermediates both in cell culture and in mice, see e. g. Abstract. Seven RNAi target sequences were chosen on the basis of their **conservation** among the major HBV genotypes. McCaffrey shows that each shRNA targets the HBV pregenomic RNA, as well as the mRNA for

the core antigen and the polymerase, and the X region and its transcript, and can inhibit HBV in cell cultures, see Fig. 2. The siRNA (dsRNA effector molecule) is encoded by the nucleic acids in the U6 shRNA expression cassette (RNA polymerase III promoters), see e.g. Fig. 1. The predicted folding of RNAi *in vivo* is shown in Fig. 1c. McCaffrey shows that RNAi effectively inhibited replication initiation in cultured cells and mammalian liver, suggesting that such an approach could be useful in the treatment of viral diseases, see e.g. Abstract.

26. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use two dsRNA comprises an at least 19 contiguous base pair nucleotide sequence from within SEQ ID NO: 3 and SEQ ID NO: 10 for inhibiting HBV *in vivo*. In the recently decided case of *KSR International Co. v. Teleflex Inc.* (82 U.S.P.Q. 2d1385, 2007), the Supreme Court provided a number of bases on which a claimed invention may be found obvious. In particular, "When there is a design need or market pressure to solve a problem and there are a finite number of identified predictable potential solutions, a person of ordinary skill has good reason to pursue the known potential options within his or her technical grasp. **If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense**".

27. In the present case, the prior art has provided a finite number of identified predictable potential solutions for the claimed method of inhibiting HBV *in vivo* using dsRNA molecules. Specifically, Ill teaches that an expression plasmid encoding **one** or **more** antisense transcripts (dsRNA effector molecule), which comprises the claimed SEQ ID NO: 10, can inhibit HBV production in mice. Sallberg teaches HBV nucleic acid-based antigen SEQ ID NO: 14, and its fragments, which comprises the claimed dsRNA effector molecule comprising SEQ ID NO: 3,

can be used for inhibiting HBV *in vivo*. McCaffrey shows that each shRNA (dsRNA) targets the HBV pregenomic RNA, the mRNA for the core antigen and the polymerase, as well as the X region and its transcript, can inhibit HBV in cell culture. McCaffrey also demonstrated that dsRNA is capable of inhibiting HBV replication in mice. Based on the prior art teachings, those of ordinary skill in the art would have had a reasonable expectation of success in using two dsRNA comprising SEQ ID NO: 3 and 10 for inhibiting HBV *in vivo*. In turn, because the claimed oligonucleotides have the properties predicted by the prior art, it would have been obvious to make such dsRNA effector molecules for inhibiting HBV *in vivo*. Therefore, the combined teachings of these references render the claimed invention obvious.

Remarks

28. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648

Notice of References Cited	Application/Control No. 10/560,377	Applicant(s)/Patent Under Reexamination PACHUK ET AL.	
	Examiner BO PENG	Art Unit 1648	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,843,770	12-1998	Ill et al.	435/320.1
*	B	US-2002/0155124	10-2002	Sallberg et al.	424/189.1
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

PATENT

IFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Catherine J. PACHUK *et al.* Confirmation No.: 3823

Application No.: 10/560,377 Group Art Unit: *To Be Assigned*

Int'l. Filing Date: June 10, 2004 Examiner: *To Be Assigned*

For: **Conserved HBV and HCV Sequences Useful for Gene Silencing**

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, **Mail Stop Amendment**
Randolph Building
401 Dulany Street
Alexandria, VA 22314

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97(b)

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicant(s) hereby submits the following information in conformance with 37 C.F.R. §§1.97 and 1.98.

[x] Pursuant to 37 C.F.R. §1.98, copies of documents 1-3 cited in the attached Form PTO-1449 are enclosed.

[ ] Copies of the remaining publications listed on the attached Form PTO-1449 are not being provided pursuant to 37 C.F.R. §1.98(d) because the publications were previously cited by or submitted to the Office in prior Application Serial Nos.:

to which the above-identified application claims priority under 35 U.S.C. §120.

[ ] Copies of documents that were not submitted in the above-mentioned related United States Patent Applications may be found in related United States Patent Application Nos.:

Should the Examiner be unable to locate a document, a copy will be provided upon request.

[ ] No copies of any U.S. patents or U.S. patent application publications listed on the attached Form PTO-1449 are being provided pursuant to 37 C.F.R. §1.98.

4

[ ] Document ___ is the PCT Patent publications of Applicants' related PCT Application no. _____, filed _____.

[x] Documents 1 and 2 were cited in a Search Report mailed September 16, 2005 (cited herein as document 3), in Applicants' related PCT patent application no. PCT/US2004/019229, filed June 10, 2004.

[x] Document 3 is an official communications from a foreign patent office received in Applicants' related PCT Application no. PCT/US2004/019229, filed June 10, 2004.

[ ] Documents _____ submitted herewith were not cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, no item of information contained in the Information Disclosure Statement was known to any individual designated in 37 C.F.R. §1.56(c) more than three months prior to the filing date of the Information Disclosure Statement.

[ ] Enclosed is a copy of a non-English publication(s) ___. Pursuant to §609 of the M.P.E.P., Applicant submits the attached foreign search or examination report, which cites such non-English language publication(s).

[ ] Enclosed is a copy of a non-English publication(s) ___. English language publication ___ (copy enclosed) claims priority from this non-English publication.

[ ] Enclosed are abstracts of non-English publications _____, cited herein as documents _____ respectively. English abstracts are attached to each document. An English abstract of non-English publication _____, document _____, may be found on the cover page of the publication.

[ ] Enclosed is an English translation of non-English publications _____, cited herein as documents _____ respectively. English translations are attached to each document.

[ ] The Examiner's attention is directed to related co-pending United States Patent Application Serial Nos.:

_____, filed _____, cited herewith as _____; and

_____, filed _____, cited herewith as _____.

This Information Disclosure Statement is filed within any one of the following time periods:

[ ] within three months from the filing date of this national application other than a CPA under 37 C.F.R. § 1.53(d);

[ ] within three months from the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in this international application;

[x] before the mailing date of a first office action on the merits; or

[ ] before the mailing of a first office action after the filing of a request for continued examination under 37 C.F.R. § 1.114.

It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Form PTO-1449 to the undersigned. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 50-1283.

Dated: March 21, 2007

Respectfully submitted,
COOLEY GODWARD KRONISH LLP

By: _____
Bonnie Weiss McLeod
Reg. No. 43,255

USPTO Customer No. 58249
COOLEY GODWARD KRONISH LLP
ATTN: Patent Group
The Bowen Building
875 15th Street, NW Suite 800
Washington, DC 20005-2221
Phone: (202) 842-7800
Fax: (202) 842-7899

INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Attorney Docket No. NUCL-006/01US	Application No. 10/560,377 (US Nat'l. Stage of PCT/US04/19229)
	Applicants: Catherine J. PACHUK *et al.*	PAGE 1 of 1
PTO Form 1449	Int'l. Filing Date: June 10, 2004	Group Art Unit: *To Be Assigned*

U.S. PATENT DOCUMENTS

Initial		Document No.	Date	Name	Class	Sub-Class	Filing Date

FOREIGN PATENT DOCUMENTS

		Document No.	Date	Country	Class	Sub-Class	Translation
/B.P./	1.	WO 03/070918 A2	08/28/2003	WIPO			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

/B.P./	2.	Holen et al., "Similar behaviour of single-strand and double-strand siRNAs suggests they act through a common RNAi pathway," Nucl. Acids Res. 31:2401-2407 (2003).
/B.P./	3.	Macchia, "International Search Report," from PCT/US2004/019229, filed June 10, 2004, 8 pages, European Patent Office, Rijswijk, The Netherlands (mailed September 16, 2005).

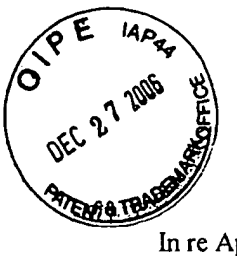
Examiner	Date Considered
/Bo Peng/	06/18/2009

Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

IFW

PATENT

Attorney Docket No. NUCL-006/01US
Application No. 10/560,377
(US Nat'l. Stage of PCT/US04/19229



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Catherine J. PACHUK *et al.* Confirmation No.: 3823

Application No.: 10/560,377 Group Art Unit: *To Be Assigned*

Int'l. Filing Date: June 10, 2004 Examiner: *To Be Assigned*

For: **Conserved HBV and HCV Sequences Useful for Gene Silencing**

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, **Mail Stop Amendment**
Randolph Building
401 Dulany Street
Alexandria, VA 22314

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97(b)

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicant(s) hereby submits the following information in conformance with 37 C.F.R. §§1.97 and 1.98.

[x] Pursuant to 37 C.F.R. §1.98, copies of documents 2-13 cited in the attached Form PTO-1449 are enclosed.

[ ] Copies of the remaining publications listed on the attached Form PTO-1449 are not being provided pursuant to 37 C.F.R. §1.98(d) because the publications were previously cited by or submitted to the Office in prior Application Serial Nos.:

to which the above-identified application claims priority under 35 U.S.C. §120.

[ ] Copies of documents that were not submitted in the above-mentioned related United States Patent Applications may be found in related United States Patent Application Nos.:

Should the Examiner be unable to locate a document, a copy will be provided upon request.

[x] No copies of any U.S. patents or U.S. patent application publications listed on the attached Form PTO-1449 are being provided pursuant to 37 C.F.R. §1.98.

[x] Document 2 is the PCT Patent publications of Applicants' related PCT Application no. PCT/US04/19229, filed June 10, 2004.

[x] Documents 1 and 5-13 were cited in a Search Report mailed October 12, 2006 (cited herein as document 4), in Applicants' related SG Application no. 200507781-3.

[x] Documents 3 and 4 are official communications from foreign patent offices received in Applicants' related SG Application no. 200507781-3.

[ ] Documents _____ submitted herewith were not cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, no item of information contained in the Information Disclosure Statement was known to any individual designated in 37 C.F.R. §1.56(c) more than three months prior to the filing date of the Information Disclosure Statement.

[ ] Enclosed is a copy of a non-English publication(s) ___. Pursuant to §609 of the M.P.E.P., Applicant submits the attached foreign search or examination report, which cites such non-English language publication(s).

[ ] Enclosed is a copy of a non-English publication(s) ___. English language publication ___ (copy enclosed) claims priority from this non-English publication.

[ ] Enclosed are abstracts of non-English publications _____, cited herein as documents _____ respectively. English abstracts are attached to each document. An English abstract of non-English publication _____, document _____, may be found on the cover page of the publication.

[ ] Enclosed is an English translation of non-English publications _____, cited herein as documents _____ respectively. English translations are attached to each document.

[ ] The Examiner's attention is directed to related co-pending United States Patent Application Serial Nos.:

_____, filed _____, cited herewith as _____; and

_____, filed _____, cited herewith as _____.

This Information Disclosure Statement is filed within any one of the following time periods:

[ ] within three months from the filing date of this national application other than a CPA under 37 C.F.R. § 1.53(d);

[ ] within three months from the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in this international application;

[x] before the mailing date of a first office action on the merits; or

[ ] before the mailing of a first office action after the filing of a request for continued examination under 37 C.F.R. § 1.114.

It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Forms PTO-1449 to the undersigned. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 50-1283.

Dated: Dec. 26, 2006

Respectfully submitted,
COOLEY GODWARD KRONISH LLP

By: _____
Bonnie Weiss McLeod
Reg. No. 43,255

USPTO Customer No. 58249
COOLEY GODWARD KRONISH LLP
ATTN: Patent Group
The Bowen Building
875 15th Street, NW Suite 800
Washington, DC 20005-2221
Phone: (202) 842-7800
Fax: (202) 842-7899

INFORMATION DISCLOSURE CITATION (Use several sheets if necessary) PTO Form 1449	Attorney Docket No. NUCL-006/01US	Application No. 10/560,377 (US Nat'l. Stage of PCT/US04/19229)
	Applicants: Catherine J. PACHUK *et al.*	PAGE 1 of 1
	Int'l. Filing Date: June 10, 2004	Group Art Unit: *To Be Assigned*

U.S. PATENT DOCUMENTS

Initial		Document No.	Date	Name	Class	Sub-Class	Filing Date
/B.P./	1.	6,518,417	02/11/2003	Sczakiel *et al.*			

FOREIGN PATENT DOCUMENTS

		Document No.	Date	Country	Class	Sub-Class	Translation
/B.P./	2.	WO 2005/014806	02/17/2005	WIPO			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

/B.P./	3.	Mackenzie, "Written Opinion," from SG 200507781-3, filed June 10, 2004, 6 pages, Australian Patent Office (mailed October 12, 2006).
	4.	Mackenzie, "Search Report," from SG 200507781-3, filed June 10, 2004, 7 pages, Australian Patent Office (mailed October 12, 2006).
	5.	Andino, "RNAi puts a lid on virus replication," *Nat. Biotechnol* **21(6)**:629-630 (2003).
	6.	Couzin, "Mini RNA Molecules Shield Mouse Liver From Hepatitis," *Science* **299**:995 (2003).
	7.	Hamasaki *et al.*, "Short interfering RNA-directed inhibition of hepatitis B virus replication," *FEBS Letters* **543**:-51-54 (2003).
	8.	Kapadia *et al.*, "Interference of hepatitis C virus RNA replication by short interfering RNAs," *Proc. Natl. Acad. Sci. USA* **100(4)**:2014-2018 (2003).
	9.	McCaffrey *et al.*, "RNA interference in adult mice," *Nature* **418**:38-39 (2002).
	10.	McCaffrey *et al.*, "Inhibition of hepatitis B virus in mice by RNA interference," *Nat. Biotechnol.* **21(6)**:639-644 (2003).
	11.	Seo *et al.*, "Small Interfering RNA-Mediated Inhibition of Hepatitis C Virus Replication in the Human Hepatoma Cell Line Huh-7," *J. Virol.* **77(1)**:810-812 (2003).
	12.	Shlomai and Shaul, "Inhibition of Hepatitis B Virus Expression and Replication by RNA Interference," *Hepatology* 37:764-770 (2003).
↓	13.	Wilson *et al.*, "RNA interference blocks gene expression and RNA synthesis from hepatitis C replicons propagated in human liver cells," *Proc. Natl. Acad. Sci. USA* **100(5)**:2783-2788 (2003).

Examiner	/Bo Peng/	Date Considered	06/18/2009

Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Please type a plus sign (+) inside this box → [+]

PTO/SB/08A (07-05)
Approved for use through 07/31/2006. OMB 0651-0031

Substitute for form 1449A/PTO		*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Application Number	10/560,377
		Filing Date	June 19, 2006
		First Named Inventor	Catherine J. Pachuk et al.
(use as many sheets as necessary)		Group Art Unit	
		Examiner Name	
Sheet	1 of 1	Attorney Docket Number	NUCL-006/01US

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-			
		US-			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3] Number[4] Kind Code[5] (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[2]
/B.P./	B1	WO 04/078181 (A1)	09-16-2004	CAPITAL BIOCHIP COMPANY, LTD. & TSINGHUA UNIVERSITY		

OTHER – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
/B.P./	C1	European Search Report based on European Patent Application No. 04776661.3, (January 14, 2008).	

Examiner Signature	/Bo Peng/	Date Considered	06/18/2009

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. [1]Unique citation designation number (optional). [2]See attached Kinds of U.S. Patent Documents. [3]Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4]For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5]Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [6]Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Catherine J. PACHUK *et al.* Confirmation No.: 3823

Application No.: 10/560,377 Group Art Unit: *To Be Assigned*

Int'l. Filing Date: June 10, 2004 Examiner: *To Be Assigned*

For: **Conserved HBV and HCV Sequences Useful for Gene Silencing**

Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, **Mail Stop Amendment**
Randolph Building
401 Dulany Street
Alexandria, VA 22314

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. §1.97(b)

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicant(s) hereby submits the following information in conformance with 37 C.F.R. §§1.97 and 1.98.

[x] Pursuant to 37 C.F.R. §1.98, copies of documents 1-3 cited in the attached Form PTO-1449 are enclosed.

[ ] Copies of the remaining publications listed on the attached Form PTO-1449 are not being provided pursuant to 37 C.F.R. §1.98(d) because the publications were previously cited by or submitted to the Office in prior Application Serial Nos.:

to which the above-identified application claims priority under 35 U.S.C. §120.

[ ] Copies of documents that were not submitted in the above-mentioned related United States Patent Applications may be found in related United States Patent Application Nos.:

Should the Examiner be unable to locate a document, a copy will be provided upon request.

[ ] No copies of any U.S. patents or U.S. patent application publications listed on the attached Form PTO-1449 are being provided pursuant to 37 C.F.R. §1.98.

[ ] Document __ is the PCT Patent publications of Applicants' related PCT Application no. _____, filed _____.

[x] Documents 2 and 3 were cited in an International Preliminary Report On Patentability mailed January 31, 2007 (cited herein as document 1), in Applicants' related PCT Application no. PCT/US04/19229.

[x] Document 1 is an official communication from a foreign patent office received in Applicants' related PCT Application no. PCT/US04/19229.

[ ] Documents _____ submitted herewith were not cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, no item of information contained in the Information Disclosure Statement was known to any individual designated in 37 C.F.R. §1.56(c) more than three months prior to the filing date of the Information Disclosure Statement.

[ ] Enclosed is a copy of a non-English publication(s) ___. Pursuant to §609 of the M.P.E.P., Applicant submits the attached foreign search or examination report, which cites such non-English language publication(s).

[ ] Enclosed is a copy of a non-English publication(s) ___. English language publication ___ (copy enclosed) claims priority from this non-English publication.

[ ] Enclosed are abstracts of non-English publications _____, cited herein as documents _____ respectively. English abstracts are attached to each document. An English abstract of non-English publication _____, document _____, may be found on the cover page of the publication.

[ ] Enclosed is an English translation of non-English publications _____, cited herein as documents _____ respectively. English translations are attached to each document.

[ ] The Examiner's attention is directed to related co-pending United States Patent Application Serial Nos.:

_____, filed _____, cited herewith as _____; and

_____, filed _____, cited herewith as _____.

This Information Disclosure Statement is filed within any one of the following time periods:

[ ] within three months from the filing date of this national application other than a CPA under 37 C.F.R. § 1.53(d);

[ ] within three months from the date of entry of the national stage as set forth in 37 C.F.R. §1.491 in this international application;

[x] before the mailing date of a first office action on the merits; or

[ ] before the mailing of a first office action after the filing of a request for continued examination under 37 C.F.R. § 1.114.

It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Forms PTO-1449 to the undersigned. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 50-1283.

Dated: Feb. 27, 2007

Respectfully submitted,
COOLEY GODWARD KRONISH LLP

By: Bonnie Weiss McLeod

Bonnie Weiss McLeod
Reg. No. 43,255

USPTO Customer No. 58249
COOLEY GODWARD KRONISH LLP
ATTN: Patent Group
The Bowen Building
875 15th Street, NW Suite 800
Washington, DC 20005-2221
Phone: (202) 842-7800
Fax: (202) 842-7899

INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Attorney Docket No. NUCL-006/01US	Application No. 10/560,377
PTO Form 1449	Applicants: Catherine J. PACHUK *et al.*	PAGE 1 of 1
	Int'l. Filing Date: June 10, 2004	Group Art Unit: *To Be Assigned*

U.S. PATENT DOCUMENTS

Initial		Document No.	Date	Name	Class	Sub-Class	Filing Date

FOREIGN PATENT DOCUMENTS

		Document No.	Date	Country	Class	Sub-Class	Translation

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

/B.P./	1.	Ford, "International Preliminary Report On Patentability," from PCT/US04/19229, filed June 10, 2004, 5 pages, United States Patent and Trademark Office, IPEA/US, (mailed January 31, 2007).
/B.P./	2.	Giladi *et al.*, "Small Interfering RNA Inhibits Hepatitis B Virus Replication in Mice," *Mol. Ther.* **8(5)**:769-776 (2003).
/B.P./	3.	Randall *et al.*, "Clearance of replicating hepatitis C virus replicon RNAs in cell culture by small interfering RNAs," *Proc. Natl. Acad. Sci. USA* **100(1)**:235-240 (2003).

Examiner	/Bo Peng/	Date Considered	06/18/2009

Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

```
<!--StartFragment-->RESULT 2  SEQ ID NO:10
US-08-613-861-1
; Sequence 1, Application US/08613861
; Patent No. 5843770
;  GENERAL INFORMATION:
;    APPLICANT:  Ill, Charles R. et al.
;    TITLE OF INVENTION:  Antisense Constructs Directed Against Viral Post-Transcriptio
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite 510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/613,861
;      FILING DATE:  13-APR-1994
;      CLASSIFICATION:  514
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/111,111
;      FILING DATE:  12-DEC-1909
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Attorney, Name Init
;      REGISTRATION NUMBER:  000000
;      REFERENCE/DOCKET NUMBER:  oe
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617)227-7400
;      TELEFAX:  (617)227-5941
;  INFORMATION FOR SEQ ID NO:  1:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  587 base pairs
;      TYPE:  nucleic acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  cDNA
US-08-613-861-1

  Query Match             100.0%;  Score 66.8;  DB 2;  Length 587;
  Best Local Similarity   92.9%;  Pred. No. 8.6e-15;
  Matches   65;  Conservative    5;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CTGCCAACTGGATHCTHCGCGGGACGTCCTTTGTYTACGTCCCGTCRGCGCTGAATCCHG 60
              ||||||||||||||:|||:||||||||||||||||||:||||||||||:||||||||||:|
Db        277 CTGCCAACTGGATCCTTCGCGGGACGTCCTTTGTTTACGTCCCGTCGGCGCTGAATCCCG 336

Qy         61 CGGACGACCC 70
              ||||||||||
Db        337 CGGACGACCC 346
<!--EndFragment-->
```

<!--StartFragment-->RESULT 8 SEQ ID NO:3
US-10-104-966-14
; Sequence 14, Application US/10104966
; Patent No. 6680059
; GENERAL INFORMATION:
; APPLICANT: Matti Sallberg
; APPLICANT: Catharina Hultgren
; TITLE OF INVENTION: VACCINES CONTAINING RIBAVIRIN AND
; TITLE OF INVENTION: METHODS OF USE THEREOF
; FILE REFERENCE: TRIPEP.23AUSC1
; CURRENT APPLICATION NUMBER: US/10/104,966
; CURRENT FILING DATE: 2002-03-22
; PRIOR APPLICATION NUMBER: 09/705,547
; PRIOR FILING DATE: 2000-11-03
; PRIOR APPLICATION NUMBER: 60/229,175
; PRIOR FILING DATE: 2000-08-29
; NUMBER OF SEQ ID NOS: 15
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 14
; LENGTH: 3182
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Hepatitis B virus sequence
US-10-104-966-14

Query Match 100.0%; Score 188.6; DB 3; Length 3182;
Best Local Similarity 85.9%; Pred. No. 8.6e-50;
Matches 177; Conservative 24; Mismatches 5; Indels 0; Gaps 0;

```
Qy          1 AAGGCCTTTCTVHGTMAACARTAYMTGMMCCTTTACCCCGTTGCYMGGCAACGGYCHGGY 60
              ||||||||||||::||:||||:||::||::|||||||||||||||::||||||||:|:||:
Db       1113 AAGGCCTTTCTGTGTAAACAATACCTGAACCTTTACCCCGTTGCCCGGCAACGGCCAGGT 1172

Qy         61 CTNTGCCAAGTGTTTGCTGACGCAACCCCCACTGGHTGGGGCTTGGYBATNGGCCATCRS 120
              || ||||||||||||||||||||||||||||||||:||||||||||::|| |||||||::
Db       1173 CTGTGCCAAGTGTTTGCTGACGCAACCCCCACTGGCTGGGGCTTGGTCATGGGCCATCAG 1232

Qy        121 CGCATGCGTGGAACCTTTBNGKCTCCTCTGCCGATCCATACTGCGGAACTCCTNGCNGCB 180
              ||||||||||||||||||: |:|||||||||||||||||||||||||||||| || ||:
Db       1233 CGCATGCGTGGAACCTTTTCGGCTCCTCTGCCGATCCATACTGCGGAACTCCTAGCCGCT 1292

Qy        181 TGTTTYGCTCGCAGCMGGTCTGGRGC 206
              |||||:|||||||||:|||||||:||
Db       1293 TGTTTTGCTCGCAGCAGGTCTGGAGC 1318
```

<!--EndFragment-->